
PART VI SUMMARY OF ACTIVITIES IN THE RISK MANAGEMENT PLAN BY MEDICINAL PRODUCT

VI.1 Elements for summary tables in the EPAR

VI.1.1 Summary table of safety concerns

Summary of safety concerns	
Important identified risks	None
Important potential risks	None
Missing information	None

VI.1.2 Table of on-going and planned studies in the Post-authorisation Pharmacovigilance Development Plan

Not applicable

VI.1.3 Summary of post-authorisation efficacy development plan

Not applicable

VI.1.4 Summary table of risk minimisation measures

As there are no safety concerns for cholecalciferol there are no risk minimization measures.

VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Vitamin D deficiency

Vitamin D deficiency appears to be a widespread global problem common in all age groups. Estimates suggest that up to 1 billion people around the world may have vitamin D deficiency or insufficiency. A high frequency of vitamin D deficiency has also been reported in infants, children, and adolescents from diverse countries around the world. There are two different forms of vitamin D, vitamin D2 and D3. Humans obtain vitamin D from dietary foods and supplements, or produced by the body. Dietary sources of vitamin D include fatty fish and foods enriched with vitamin D2 or D3, like dairy products, infant formula (manufactured food designed and marketed for feeding to babies and infants under 12 months of age), and breakfast cereal.¹



Vitamin D deficiency causes rickets (condition in which bones become soft and weak, which can lead to bone deformities) in children and will precipitate and exacerbate osteopenia (weak bones), osteoporosis (low bone density), and fractures in adults.²

The National Health and Nutrition Examination Survey 2005 to 2006 data analyzed for vitamin D levels in adult participants shows that overall occurrence rate of vitamin D deficiency was 41.6%, with the highest rate seen in Blacks (82.1%), followed by Hispanics (69.2%). Vitamin D deficiency was significantly more common among those who had no college education, were obese (overweight), with a poor health status, hypertension, low high-density lipoprotein cholesterol level, or not consuming milk daily.³

Osteoporosis

Osteoporosis is a bone disease in which mass and density of bone decreases and there are more chances of fractures. Currently, more than 10 million people in the United States are affected by osteoporosis and it is believed that approximately 14 million adults over the age of 50 by the year 2020 will be affected. Also around 200 million women have osteoporosis worldwide.⁴

Osteoporosis is responsible for more than 1.5 million fractures annually including 300,000 hip fractures, approximately 700,000 vertebral fractures, 250,000 wrist fractures, and more than 300,000 fractures at other sites. The lifetime risk for any fragility fractures in Caucasian women at age 50 years approaches 40% and 13% in men. About 17% of postmenopausal White women in the United States have osteoporosis.⁵

VI.2.2 Summary of treatment benefits

Vitamin D deficiency

Vitamin D is a fat soluble nutrient which is important for skeletal and non-skeletal health. Worldwide, vitamin D is obtained through exposure to UVB (Ultraviolet B) radiation in the form of sunlight and cutaneous (skin) vitamin D production. Latitude, cultural dress habits, season, avoiding sun, and sunscreen protection can all limit vitamin D production. Stomach, liver, and kidney disease may be related to low vitamin D levels, but hypovitaminosis D (low vitamin D level) most commonly results from inadequate intake. Low vitamin D level which has been resulted from lack of UVB exposure is not easily treated by diet. Supplements are necessary to correct this condition.⁶

Vitamin D deficiency can be treated by providing vitamin D through mouth or by injection in the muscles, together with enough elemental calcium to prevent low level of calcium that may be associated with remineralisation of the bone. The three oral forms of vitamin D that are available are ergocalciferol (Vitamin D2), cholecalciferol (Vitamin D3), and calcitriol. Vitamin D2 and D3 are available in a concentrated syrup formulation useful for infants and young children. Calcitriol is not a first line treatment for vitamin D deficiency, because it directly effects kidneys and increases the risk of stones in the gall bladder and high calcium levels. While both vitamin D2 and D3 have been used to treat vitamin D deficiency rickets in infants and children.¹

Osteoporosis

Bisphosphonates (such as alendronate sodium or risedronate) are considered appropriate initial choices for osteoporosis. Bisphosphonates increase BMD (bone mineral density). Adequate calcium and vitamin D are important for maintaining bone health and for the effectiveness of therapy. Most of the clinical data suggest significant clinical improvements in response to combination therapies versus monotherapy in postmenopausal osteoporosis.⁷

Cholecalciferol with either alendronate (medicine to treat osteoporosis) or calcium corrects vitamin D deficiency and improves the outcome of therapy in osteoporotic patients by increasing the strength of bones. The benefits include reduction in frequencies of falling and bone fractures in osteoporotic women. The benefits are further increased when higher doses of cholecalciferol are used.⁷

Vitamin D deficiency is more common in children, the elderly and women. It has been estimated that 1 billion people worldwide have vitamin D deficiency. A recent survey in the UK showed that more than 50% of the adult population has insufficient levels of vitamin D and that 16% have severe deficiency during winter and spring.⁸

VI.2.3 Unknowns relating to treatment benefits

There is no information available regarding the effects of this medicine in pregnancy.

VI.2.4 Summary of safety concerns

Important identified risks

There are no important identified risks associated with cholecalciferol

Important potential risks

There are no important potential risks associated with cholecalciferol.

VI.2.5 Summary of risk minimisation measures by safety concern

There are no important risks associated with cholecalciferol.

VI.2.6 Planned post-authorisation development plan

Not applicable

VI.2.7 Summary of changes to the risk management plan over time

This is the first risk management plan for Cholecalciferol 400 IU soft capsules.